SUPPLEMENTARY MATERIAL

Supplementary methods

Exclusion criteria

Patients who have received autologous hematologic stem cell transplant; history of inflammatory bowel disease, celiac disease, prior gastrectomy or upper bowel removal, or any other gastrointestinal disorder that would interfere with the absorption, distribution, metabolism, or excretion of CC-90010 and/or predispose the patient to an increased risk of gastrointestinal toxicity; prior history of unstable central nervous system metastases; impaired cardiac function or clinically significant cardiac diseases; or history of concurrent secondary cancers requiring ongoing systemic treatment.

Dose-limiting toxicity

Patients were considered evaluable for dose-limiting toxicity (DLT) if they experienced a DLT after receiving ≥1 dose of study treatment or received ≥80% of the total planned dose amount of CC-90010 during cycle 1 without experiencing a DLT. Dosing was interrupted if any treatment-related grade ≥2 toxicities were not resolved to grade ≤1 prior to the next dose.

The DLT period was cycle 1 (28 days) and were defined as the following: grade 2 fasting hyperglycemia lasting >14 days despite optimal medical treatment; grade ≥3 fasting hyperglycemia (>250 mg/dL) lasting >4 days; grade 4 hyperglycemia lasting ≥12 hours despite adequate treatment; hyperglycemia associated with diabetic ketoacidosis or nonketotic hyperosmolar coma regardless of glucose level; hyperglycemia that necessitated dose reduction despite dose interruption and resolution to grade ≤1 hyperglycemia within 2 weeks; any grade 4 nonhematologic toxicity of any duration; any nonhematologic grade ≥3 toxicity except: grade 3 diarrhea, nausea, or vomiting lasting ≤3 days,

grade 3 rash of the acneiform, pustular or maculopapular type or fatigue which resolves to grade ≤2 within 7 days of CC-90010 interruption; febrile neutropenia or grade 4 neutropenia lasting >7 days; grade 4 thrombocytopenia lasting >7 days, grade ≥3 thrombocytopenia with clinically significant bleeding. Hematological toxicities included febrile neutropenia, grade 4 neutropenia lasting >7 days, grade 4 thrombocytopenia lasting >7 days, and grade ≥3 thrombocytopenia with clinically significant bleeding. In addition, any grade ≥2 adverse event not specified necessitating a dose level reduction during cycle 1 was considered a DLT unless clearly determined to be unrelated to CC-90010. Isolated laboratory changes without associated clinical signs or symptoms (eg, hypomagnesemia, hypermagnesemia, hypoalbuminemia, hypophosphatemia, lymphocyte count increased or decreased) were not considered DLTs.

Study assessments

Blood samples for pharmacodynamic analysis were collected at baseline and 24 hours after CC-90010 dose for all three dosing schedules; at cycle 1 day1, prior to day 2, prior to day 3, day 4, day 8, and last dose in cycle 1 for weekly and biweekly dosing schedules; and at cycle 1 day 1, prior to day 2, day 4, and day 5 for the monthly dosing schedule (**Supplementary Tables 1** and **2**). Blood biomarker CCR1 levels were measured at timepoints listed in **Supplementary Tables 1** and **2** using Quantigene technology (Thermo Fisher) and normalized to the expression of the control gene, peptidylprolyl isomerase B. The data is presented as percent of pre-dose levels.

Detection of CC-90010 in the cerebrospinal fluid was assessed in a single patient enrolled in the weekly schedule (2 days on/5 days off). CSF samples were collected pre-dose and 1- and 2-hours post-dose on day 23 through a shunt or reservoir that the patient had in place. Time-matched PK blood samples were collected with the CSF samples.

Serial blood samples for PK analysis were collected for each dosing schedule after the first and last doses in cycle 1. These time points corresponded to day 23 for the weekly dosing schedules, day 17 for the biweekly dosing schedule, and day 4 for monthly dosing schedule.